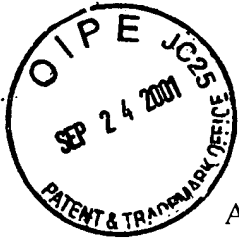


Applicant : Samir Kumar et al.
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Filed : March 30, 2000
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REMARKS

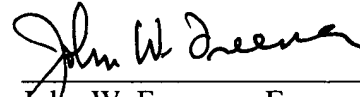
Applicants hereby submit that the enclosures fulfill the requirements under 37 C.F.R. §1.821-1.825. The amendments in the specification merely insert the paper copy of the Sequence Listing and sequence identifiers in the specification. No new matter has been added.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment.

Please apply any charges or credits to Deposit Account No. 06-1050.

Respectfully submitted,

Date: 9/20/01



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“Version With Markings to Show Changes Made”

In the specification:

Paragraph beginning at page 8, line 8, has been amended as follows:

In further embodiment the conserved peptide motifs as identified comprise:

- | | |
|--------------------------------------|------------------------------------|
| 1. AAQSIGEPGTQLT (SEQ ID NO:1) | 43. LLNRAPTLH (SEQ ID NO:43) |
| 2. AGDGTTTAT (SEQ ID NO:2) | 44. LPDKAIDLIDE (SEQ ID NO:44) |
| 3. AGRHGNKG (SEQ ID NO:3) | 45. LPGKLADS (SEQ ID NO:45) |
| 4. AHIDAGKTTT (SEQ ID NO:4) | 46. LSGGQQQR (SEQ ID NO:46) |
| 5. CPIETPEG (SEQ ID NO:5) | 47. MGHVDHGKT (SEQ ID NO:47) |
| 6. DEPSIGLH (SEQ ID NO:6) | 48. NADFDGDQMAVH (SEQ ID NO:48) |
| 7. DEPTSALD (SEQ ID NO:7) | 49. NGAGKSTL (SEQ ID NO:49) |
| 8. DEPTTALDVT (SEQ ID NO:8) | 50. NLLGKRVD (SEQ ID NO:50) |
| 9. DHAGIATQ (SEQ ID NO:9) | 51. NTDAEGR (SEQ ID NO:51) |
| 10. DHPHGGGEG (SEQ ID NO:10) | 52. PSAVGYQPTLA (SEQ ID NO:52) |
| 11. DLGGGTFD (SEQ ID NO:11) | 53. QRVAIARA (SEQ ID NO:53) |
| 12. DVLDTWFS (SEQ ID NO:12) | 54. QRYKGLGEM (SEQ ID NO:54) |
| 13. ERERGITI (SEQ ID NO:13) | 55. RDGLKPVHRR (SEQ ID NO:55) |
| 14. ERGITITSAAT (SEQ ID NO:14) | 56. SALDVSIQA (SEQ ID NO:56) |
| 15. ESRRIDNQLRGR (SEQ ID NO:15) | 57. SGGLHGVG (SEQ ID NO:57) |
| 16. FSGGQRQR (SEQ ID NO:16) | 58. SGSGKSSL (SEQ ID NO:58) |
| 17. GEPGVGKTA (SEQ ID NO:17) | 59. SGSGKSTL (SEQ ID NO:59) |
| 18. GFDYLRDN (SEQ ID NO:18) | 60. SVFAGVGERTREGND (SEQ ID NO:60) |
| 19. GHNLEQHS (SEQ ID NO:19) | 61. TGRTHQIRVH (SEQ ID NO:61) |
| 20. GIDLGTNS (SEQ ID NO:20) | 62. TGVSGSGKS (SEQ ID NO:62) |
| 21. GINLLREGLD (SEQ ID NO:21) | 63. TLSGGEAQRI (SEQ ID NO:63) |
| 22. GIVGLPNVGKS (SEQ ID NO:22) | 64. TNKYAEGYP (SEQ ID NO:64) |
| 23. GKSSLLNA (SEQ ID NO:23) | 65. TPRSHPATY (SEQ ID NO:65) |
| 24. GLTGRKIIVDTYG (SEQ ID NO:24) | 66. VEGDSAGG (SEQ ID NO:66) |
| 25. GPPGTGKTLA (SEQ ID NO:25) | 67. VRKRPGMYIG (SEQ ID NO:67) |
| 26. GPPGVGKT (SEQ ID NO:26) | |
| 27. GSGKTTLL (SEQ ID NO:27) | |
| 28. GTRIFGPV (SEQ ID NO:28) | |
| 29. IDTPGHVDFT (SEQ ID NO:29) | |
| 30. IIAHIDHGKSTL (SEQ ID NO:30) | |
| 31. INGFRIGR (SEQ ID NO:31) | |
| 32. IREGGRTVG (SEQ ID NO:32) | |
| 33. IVGESGSGKS (SEQ ID NO:33) | |
| 34. KFSTYATWWI (SEQ ID NO:34) | |
| 35. KMSKSKGN (SEQ ID NO:35) | |
| 36. KMSKSLGN (SEQ ID NO:36) | |
| 37. KNMITGAAQMDGAILVV (SEQ ID NO:37) | |
| 38. KPNSALRK (SEQ ID NO:38) | |
| 39. LFGGAGVGKTV (SEQ ID NO:39) | |
| 40. LGPSGCGK (SEQ ID NO:40) | |
| 41. LHAGGKFD (SEQ ID NO:41) | |
| 42. LIDEARTPLIISG (SEQ ID NO:42) | |

Paragraph beginning at page 12, line 23, has been amended as follows:

Figure 4 shows crystal structures of three invariant peptides (**VRKRPGMYIG** (SEQ ID NO:67), **LHAGGKFD** (SEQ ID NO:41) and **SGGLHGVG** (SEQ ID NO:57)) from DNA gyrase B protein.

Paragraph beginning at page 13, line 22, has been amended as follows:

Downloaded Files and their format:

<organism_name>. pep : file which stores the annotation & the protein sequence

<organism-name> refers to

Tb (*Mycobacterium tuberculosis*) **Bs** (*Bacillus subtilis*) **Mg** (*Mycoplasma genitalium*) **Mp** (*Mycoplasma pneumoniae*) **Ec** (*Escherichia coli*) **Hp** (*Helicobacter pylori*) **Hi** (*Haemophilus influenzae*)

Format: FASTA

">gi|"<annotation>
<<the entire protein sequence.....

For example,

>gi|2808711|emb|CAA16238.1|dnaA
MTDDPGSGFTTVWNAVSELNQDPKVDDGPSSDANLSAPLTPQQRAWNLVQPLTIVE
GFALLSVPSFVQNEIERHLRAPITDALSRRLGHQIQLGVRIAPPATDEADTTVPPSENP
ATTSPDTTDNDDEIDDSAAARGDNQHSWP.....(SEQ ID NO:68)

>gi|3261513|emb|CAA16239.1|dnaN
MDAATTRVGLTDLTFRLRESFADAVSWVAKNLPARPAVPVLSGVLLTGSDNGLTISGF
DYEVSAAEQVGAEIVSPGSVLVSGRLLSDITRALPNKPVDVHVEGNRVALTCGNARFSL
PTMPVEDYPTLPTLPEETGLLPAE.....(SEQ ID NO:69)

Paragraph beginning at page 15, line 17, has been amended as follows:

An invariant peptide having sequence **FSGGQRQR** (SEQ ID NO:16) was found to exist in oppF/dppF proteins of six organisms out of the seven examined (except for in *M. tuberculosis*). This protein functions as an ATP binding protein. Since this invariant peptide has also been found to be located on the hypothetical protein encoded by **Rv1273c** gene in *M.*

tuberculosis, it is suggested that this protein encoded by **Rv1273c** gene must function as ATP binding protein as it holds the signature of this class of protein.

Paragraph beginning at page 15, line 25, has been amended as follows:

Another invariant peptide having sequence **GIVGLPNVGKS** (SEQ ID NO:22) was found in proteins having GTP binding function in six bacteria out of the seven examined (except for in *M. tuberculosis*) where as the same invariant sequence is present in hypothetical protein encoded by **Rv1112** protein in *M. tuberculosis*. It is strongly suggested that this hypothetical protein may have GTP binding property as it holds the signature of this class of protein.

Paragraph beginning at page 16, line 3, has been amended as follows:

Enzyme DNA gyrase is known to reduce supercoiling of DNA. This protein is absent in human and has been considered as a potential drug target. However, the exact sequence to which the drug molecules should be targeted is not yet clear. The peptides such as **VRKRPGMYIG** (SEQ ID NO:67), **LHAGGKFD** (SEQ ID NO:41), **SGGLHGVG** (SEQ ID NO:57), **LPGKLADC** (SEQ ID NO:45), **VEGDSAGG** (SEQ ID NO:66) and **QRYKGLGEM** (SEQ ID NO:54) that are invariant across many pathogenic and non-pathogenic bacterial DNA gyrase beta subunit, but absent in host, are the structural determinants which could be used as potential drug targets against bacterial infections. The crystal structures of three of these peptides are shown in fig 4.

In the claims:

Claim 4 has been amended as follows:

4. (Amended) A method as claimed in claim 1 where conserved peptide motifs as modified comprising:

- | | |
|----------------------------------|--------------------------------------|
| 1. AAQSIGEPGTQLT (SEQ ID NO:1) | 35. KMSKSKGN (SEQ ID NO:35) |
| 2. AGDGTTTAT (SEQ ID NO:2) | 36. KMSKSLGN (SEQ ID NO:36) |
| 3. AGRHGNKG (SEQ ID NO:3) | 37. KNMITGAAQMDGAILVV (SEQ ID NO:37) |
| 4. AHIDAGKTTT (SEQ ID NO:4) | 38. KPNSALRK (SEQ ID NO:38) |
| 5. CPIETPEG (SEQ ID NO:5) | 39. LFGGAGVGKTV (SEQ ID NO:39) |
| 6. DEPSIGLH (SEQ ID NO:6) | 40. LGPSGCGK (SEQ ID NO:40) |
| 7. DEPTSALD (SEQ ID NO:7) | 41. LHAGGKFD (SEQ ID NO:41) |
| 8. DEPTTALDVT (SEQ ID NO:8) | 42. LIDEARTPLIISG (SEQ ID NO:42) |
| 9. DHAGIATQ (SEQ ID NO:9) | 43. LLNRAPTLH (SEQ ID NO:43) |
| 10. DHPHGGGEG (SEQ ID NO:10) | 44. LPDKAIDLIDE (SEQ ID NO:44) |
| 11. DLGGGTFD (SEQ ID NO:11) | 45. LPGKLADS (SEQ ID NO:45) |
| 12. DVLDTWFSS (SEQ ID NO:12) | 46. LSGGQQQR (SEQ ID NO:46) |
| 13. ERERGITI (SEQ ID NO:13) | 47. MGHVDHGKT (SEQ ID NO:47) |
| 14. ERGITITSAAT (SEQ ID NO:14) | 48. NADFDGDQMAVH (SEQ ID NO:48) |
| 15. ESRRIDNQLRGR (SEQ ID NO:15) | 49. NGAGKSTL (SEQ ID NO:49) |
| 16. FSGGQRQR (SEQ ID NO:16) | 50. NLLGKRVD (SEQ ID NO:50) |
| 17. GEPGVGKTA (SEQ ID NO:17) | 51. NTDAGRL (SEQ ID NO:51) |
| 18. GFDYLRDN (SEQ ID NO:18) | 52. PSAVGYQPTLA (SEQ ID NO:52) |
| 19. GHNLQEH (SEQ ID NO:19) | 53. QRVAIARA (SEQ ID NO:53) |
| 20. GIDLGTNS (SEQ ID NO:20) | 54. QRYKGLGEM (SEQ ID NO:54) |
| 21. GINLLREGLD (SEQ ID NO:21) | 55. RDGLKPVHRR (SEQ ID NO:55) |
| 22. GIVGLPNVGKS (SEQ ID NO:22) | 56. SALDVSIQA (SEQ ID NO:56) |
| 23. GKSSLLNA (SEQ ID NO:23) | 57. SGGLHGVG (SEQ ID NO:57) |
| 24. GLTGRKIIVDTYG (SEQ ID NO:24) | 58. SGSGKSSL (SEQ ID NO:58) |
| 25. GPPGTGKTLLA (SEQ ID NO:25) | 59. SGSGKSTL (SEQ ID NO:59) |
| 26. GPPGVGKT (SEQ ID NO:26) | 60. SVFAGVGERTREGND (SEQ ID NO:60) |
| 27. GSGKTLL (SEQ ID NO:27) | 61. TGRTHQIRVH (SEQ ID NO:61) |
| 28. GTRIFGPV (SEQ ID NO:28) | 62. TGVSGSGKS (SEQ ID NO:62) |
| 29. IDTPGHVDFT (SEQ ID NO:29) | 63. TLSGGEAQRI (SEQ ID NO:63) |
| 30. IIAHIDHGKSTL (SEQ ID NO:30) | 64. TNKYAEGYP (SEQ ID NO:64) |
| 31. INGFRIGR (SEQ ID NO:31) | 65. TPRSHPATY (SEQ ID NO:65) |
| 32. IREGGRTVG (SEQ ID NO:32) | 66. VEGDSAGG (SEQ ID NO:66) |
| 33. IVGESGSGKS (SEQ ID NO:33) | 67. VRKRPGMYIG (SEQ ID NO:67) |
| 34. KFSTYATWWI (SEQ ID NO:34) | |